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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,089	10/02/2003	Jean-Michel Bernardon	016800-437	8389

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EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,089	BERNARDON ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/002040.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are pending.

Election/Restrictions

2. In response to the restriction requirement mailed on April 2, 2004, Applicant has elected without traverse the Group II invention, i.e. Claims 21 and 22. Applicants also elect the single disclosed species of Example 4 and the prevention or treatment of a dermatological condition involving a keratinization disorder having an inflammatory and/or immunoallergic component. Claims 21-22 to the extent of the elected method of prevention or treatment of a dermatological condition involving a keratinization disorder having an inflammatory and/or immunoallergic component with the inventive compound, and new claims 23, 24, directed to the elected species method, are examined for merits. Claims of Group I invention is withdrawn from further consideration as being drawn to the non-elected invention.

Amending the claims to the elected subject matter is recommended.

Priority

3. This application is the continuation of 09/788469. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant method of prevention or treatment of a dermatological condition involving a keratinization disorder having an inflammatory and/or immunoallergic component reaches out to an as yet unidentified keratinization disorder having an inflammatory and/or immunoallergic component, the description of which is not found in the specification.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant is drawn to a method of prevention or treatment of a dermatological condition involving keratinization disorder having an inflammatory and/or immunoallergic component.

The term 'involving' is vague and indefinite as the degree of involvement required to be considered 'involved' has not been defined in the specification.

The phrase 'having an inflammatory and/or immunoallergic component' is vague and indefinite as the extent of 'the inflammatory and/or immunoallergic component' is not defined in the specification.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. *Nature of the invention.*

The instant invention is drawn to the method of prevention or treatment of a dermatological condition involving keratinization disorder having an inflammatory and/or immunoallergic component with the inventive adamantyl stilbene compound with affinity for the retinoid receptor.

b. *State of the prior art and the level of the skilled in the art.*

Retinoid receptors has two major families designated RAR and RXR, which have different subtypes and tissue distributions. Compounds similar to retinoids having retinoid-like activity have been described (Charpentier et al. J. Med. Chem. 1995, 38:4993-5006, PTO-1449). The retinoid receptor antagonist compound would counteracts the retinoic acid effects (Apfel et al. Proc. Natl. Acad. Sci. USA, 1992, 89 : 7129-7133).

While some retinoids, such as isotretinoin, etretinate and acitretin have been shown to be useful for treatment of psoriasis, and several other disorders of keratinization, the retinoid effect appears to be unsatisfactory for other keratinization disorders, such as inflammatory linear verrucous epidermal naevi, pachyonychia congenita etc. (Orfanos et al. Drugs. 1997, 53(3) : 358-370).

While treatment of some of these disorders may be feasible, the criteria for predicting those who are at risk of developing such conditions have not been established and the prevention of these conditions has not been shown.

The level of the skill in the retinoid art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability is well recognized in the retinoid receptor ligand art. A slight modification of the structure of the compound would result in drastic changes in its biological activity as evidenced in the very different Ki values in the binding assay and the different AC50 values in the F9 differentiation assay exhibited by structurally similar compounds (Charpentier, page 4988, Table 1). The affinities and activities do not strictly correlate (Charpentier, page 4999, column 2). One of ordinary skill in the art therefore would have no basis to extrapolate the results of the tested compounds to the compounds of dissimilar structures.

d. *Amount of guidance/working examples.*

The preparation of the compounds has been described. An example of the compound wherein R' and R" are independently an amino acid, peptide or sugar residue has not been described.

The specification only describes that the inventive compounds show acitivity in the test of differentiation of mouse embryonic teratocarcinoma cells (F9) and/or in the test of inhibition of ornithine decarboxylase after induction with TPA in mice. Results for the procedures for assessing the agonist activity have not been shown. Only the procedure for assessing the RAR antagonist activity in mouse embryonic F9 cell differentiation test is described in Example 25. The results are shown for Examples 2, 4, 5, 10, 7. No in vivo procedures are described.

e. *The breadth of the claims.*

Applicant's assertion that all the structurally diverse compounds (especially those whose wherein R12 or R' and R" are independently a polyhydroalkyl, or any amino acid, peptide or sugar residue, whose structures are not fully described, and they are structurally far removed from the example compounds) would be effective for preventing or treating any dermatological condition involving keratinization disorder having an inflammatory and/or immunoallergic component, does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability of the art, and the working examples limited only to antagonist activity (paragraphs c-e above).

Since retinoids, which activate the retinoid receptors, are known for treating keratinization disorder, and the retinoid receptor antagonist compounds are known to counteract

the retinoic acid effects (Apfel, abstract), one of ordinary skill in the art would not be able to use the inventive antagonist compounds (such as the 2^{nd} , 4^{th}, 5^{th}, 7^{th}, 10^{th} compound in claim 24) for preventing or treating a dermatological condition involving keratinization disorder having an inflammatory and/or immunoallergic component as recited.

f. *Quantitation of undue experimentation.*

Since insufficient teaching and guidance are provided in the disclosure (paragraphs c-e above), one of ordinary skill in the art, even with high level of skill, would not be able to use all the compounds as claimed for preventing or treating any dermatological condition involving keratinization disorder having an inflammatory and/or immunoallergic component without undue experimentation.

Conclusion

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
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Art Unit 1625